SEGMENTATION AND MODELING OF MITOCHONDRIA WITH DENSELY CONVOLUTED INNER MEMBRANES

Raquel A. Adams[1], Carmen A. Mannella[2,3], W. Jonathan Lederer[3]. M. Saleet Jafri[1,3]

[1]Krasnow Institute for Advanced Study and School of Systems Biology, George Mason University, Fairfax VA 22030, [2]Wadsworth Center, New York State Department of Health, Albany NY 12201,
[3]Center for Biomedical Engineering and Technology, University of Maryland School of Medicine, Baltimore MD 21201

INTRODUCTION

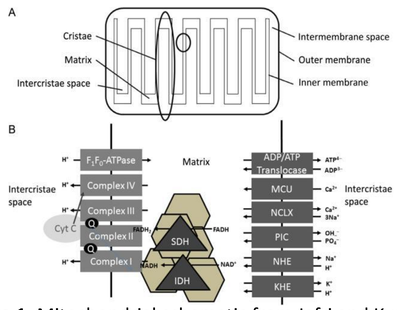


Figure 1. Mitochondrial schematic from Jafri and Kumar 2014 .

The mitochondrial cristae are folds of the mitochondrial inner membrane containing protein complexes involved in energy metabolism. The diagram above shows the different parts of a mitochondrion. In Figure 1A, the inner membrane (in oval) is shaped to maximize its surface area and the mitochondrial matrix is a viscous space within the inner membrane. The circled region is enlarged in Figure 1B. This is the site for energy metabolism containing proteins for the respiratory chain and oxidative phosphorylation located in the membrane and the tricarboxylic acid (TCA) cycle. The rest are proteins involved in the transport of substances in and out of the mitochondria. (MCU, mitochondrial calcium uniporter; NCLX, mitochondrial sodium–calcium–lithium exchanger; PIC, phosphate carrier; NHE, sodium hydrogen exchanger; KHE, potassium hydrogen exchanger).

This structure varies within different types of mitochondria and is directly tied to their function (Mannella, Lederer, and Jafri 2013). For this reason, a diseased mitochondrion can have damaging ultrastructural change and further understanding of the structure of this organelle has become crucial. Due to these disparities, it is difficult to develop a general segmentation process applicable to all mitochondrial structures but a combination of methods can build a complex mesh.

METHODS: PREPROCESSING

The initial step is capturing the mitochondria in high resolution. This is done by transmission electron microscopy (TEM) (Mannella 2006). As of now, human judgment is still necessary to analyze and select the means of method for selecting the mitochondria being segmented. This study used Microscopy Image Browser (MIB) as a segmentation platform. MIB is a software suite for high-performance segmentation and image processing of multidimensional datasets. Figure 2 Illustrates the preprocessing of the image volume. Figure 2A is the original image with an adjusted contrast. Figure 2B is the same image slice with anisotropic diffusion applied. The anisotropic diffusion is also called Perona-Malik diffusion. It eliminates noise by using an impulse function while retaining significant features of the image. Frangi filter is then used in Figure 2C. This is a Hessian-based method developed by Frangi and his group in 1999. To further eliminate noise, a median filter was used.

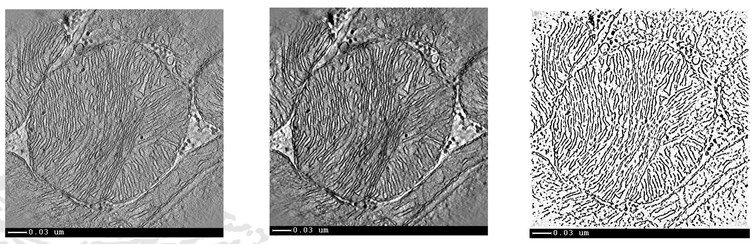


Figure 2. Preprocessing of the image volume: slice number 45.

METHODS: SEGMENTATION

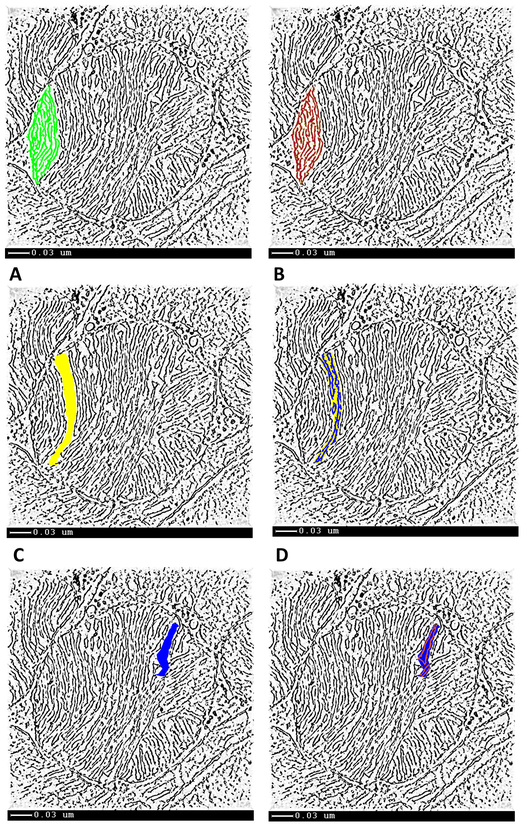
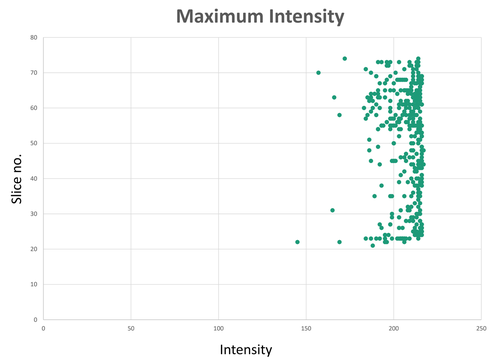


Figure 3. Selection and thresholding of images.



Plot 1. Maximum Intensity of each slice.

Figure 3 demonstrates the highlighting and thresholding of different regions. Figure 3A and 3B are region 1 of this mitochondrion. This region has cristae that are very close together. It was selected by manual tracing before thresholding. The tracing method traces each feature of this region (Figure 3A). Figure 3B shows the thresholding on top of the selection. Figure 3C and 3D are region 2. It was selected by tracing its general area manually (Figure 3C) before applying threshold (Figure 3D). Figure 3E and 3F are region 3. This crista was selected because it seems to have a wider inner cristae space. Figure 3E shows the manual selection of its general space and Figure 3F shows the thresholding on top of the selection. Plot 1 shows the maximum intensity of the segmented areas of each slice. MATLAB isosurface is then used to build the mesh.

RESULTS

Figure 4 are pictures of the 3D meshes that were built from the segmentation method from Figure 3. Figure 4A and 4B are region 1, Figure 4C and 4D are region 2, and Figure 4E and 4F are region 3. Figure 4G and 4H are the thresholding and built mesh of the whole mitochondrion respectively.

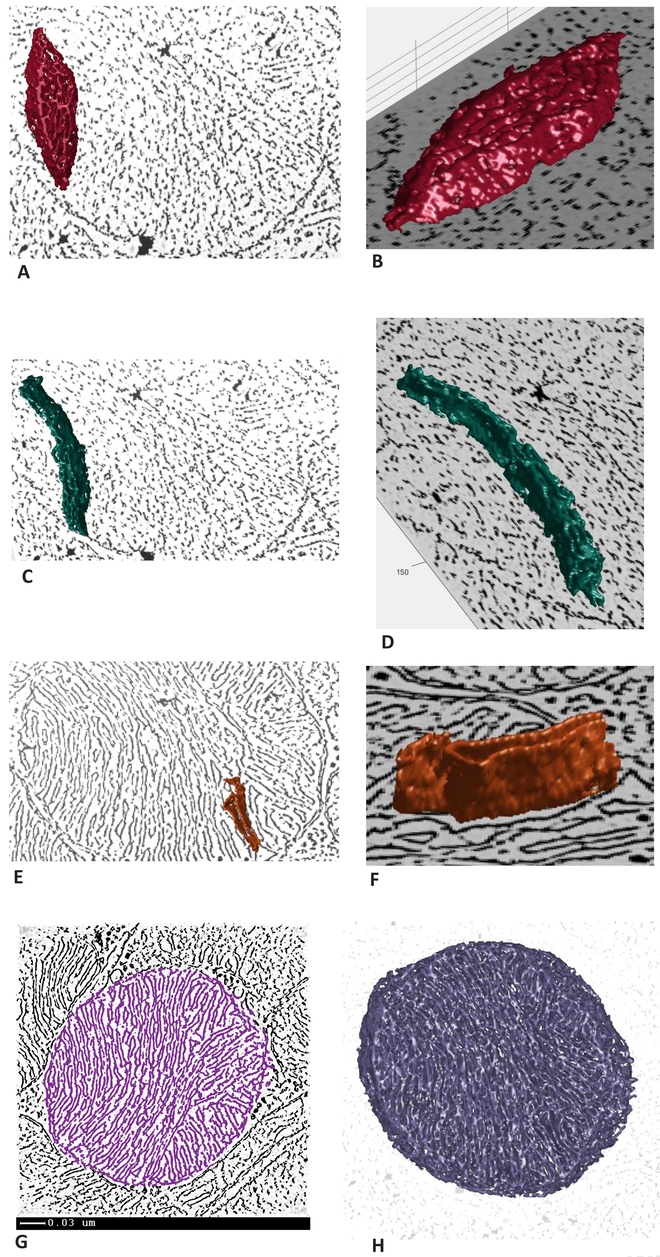


Figure 4. 3-dimensional meshes.

DISCUSSION

Whole mitochondrion can be done all at once (Figure 4G and 4H) using thresholding, but it does not always provide the necessary features and accuracy though it may be useful for studying measurements, basic shapes and structures, protein localization, and compartmentalization. Rendering the cristae by regions provides a better understanding of how one crista connect to the next. It also shows a more refined rendition of the features, such as curvature and holes within the sides of the crista. In addition, taking parts of the cristae will be more suitable for experiments and gives us a better impression of the dynamic element of this organelle at a more adjacent view. However, most mitochondrial models are simplified that spatial structure of the mitochondrion has been omitted and mathematical simulations are often acquired from steady-state experimental data. Kinetic experimental data can be used for a deeper modeling of mitochondria and a 3-dimensional mitochondrial model will aid in providing a suitable computational environment.

Acknowledgments

This project is funded by the NIH - NHLBI grant U01HL116321.

Contact

Raquel A. Adams
George Mason University
Email: radams12@gmu.edu

References

1. Belevich I, Joensuu M, Kumar D, Vihinen H, Jokitalo E. (2016) Microscopy Image Browser: A Platform for Segmentation and Analysis of Multidimensional Datasets. *PLoS Biol.* 14(1): e1002340. https://doi.org/10.1371/journal.pbio.1002340
2. Frangi AF, Niessen WJ, Hoogeveen RM, van Walsum T, Viergever MA. (1999) Model-based quantitation of 3-D magnetic resonance angiographic images. *IEEE Trans. Med. Imag.* 18:946-956.
3. Huang T, Yang G, Tang G. (1979) A fast two-dimensional median filtering algorithm. *IEEE Trans. Acoust., Speech, Signal Processing.* 27(1):13-18.
4. Jafri MS, Kumar R. (2014) Modeling Mitochondrial Function and Its Role in Disease. *Prog Mol Biol Transl Sci.* 123:103-125.
5. Mannella CA (2006) Structure and dynamics of the mitochondrial inner membrane cristae. *Biochim Biophys Acta.* 1763(5-6):542-8.
6. Mannella CA, Lederer WJ, Jafri MS (2013) The connection between inner membrane topology and mitochondrial function. *J Mol Cell Cardiol.* 62:51-57.
7. Peron P, Malik J. (1987) Scale-space and edge detection using anisotropic diffusion. *Proceedings of IEEE Computer Society Workshop on Computer Vision*. 16-22.